knowns and then all 72 of the spectra were projected onto this plane. The interesting result of this test is shown in Fig. 3, in which it can be seen that four of the hallucinogens are found to be loosely distributed in the "gray area" between the two clusters and only two are graphed with the sedatives.

It is important to note that, after selection of the 64 compounds as knowns, as in experiment 2a, the correct categorization of the remaining compounds is by no means trivial, although occasionally some correct classifications can be made by using very simple rules. Half the sedatives are in fact barbituric acid derivatives whose spectra, structures, and activities are well known. That any of these can be correctly classified comes as no surprise, but that other, structurally diverse sedatives (compounds 20, 22, 24, and 25, for example) in Table 1 have been defined as unknowns and then correctly classified is noteworthy. Compounds 19 and 30 proved to be difficult to classify unambiguously. Both were classifiable as sedatives but with less certainty than in the other cases. It is of interest here to note that there is some uncertainty surrounding the definition of tetrahydrocannabinol (compound 30) as a sedative. Further, in view of the fact that the molecular weight of the sedatives is commonly below 250 while many of the tranquilizers have molecular weights above 250, a classification on this basis would seem simple. In practice, however, five of the tranquilizers have molecular weights below 250 and four of the sedatives have molecular weights above 250. More importantly, the 30 masses with the highest Fisher ratios include only one (lowranking) member of mass greater than 250. Molecular weight is therefore of very little importance in the method developed in this way. The precise factors involved in the classification process are of great interest, and further work is needed to identify these.

Much further inquiry is suggested by this work. The pharmacological activity could, in principle, be identified by posing a series of consecutive, binary questions (for example, CNS active or not? If CNS active, depressant or stimulant? If depressant, sedative or tranquilizer? and so on) and attempting to answer these questions by using the methods described above. This would provide the basis of a general approach to the screening of compounds for pharmacological activity. A second, particularly interesting problem is that of deciphering the rules that the machine is devel-

oping in achieving the clustering. If these rules can be isolated and reexpressed in terms of mass spectral features, or even chemical structures, the way is clear to a relatively facile method of studying relationships between structure and pharmacological activity.

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- 16 November 1972; revised 5 February 1973

Visual Resolution and Experience: Acuity Deficits in **Cats Following Early Selective Visual Deprivation**

Abstract. Cats reared during the first 5 months of life in environments that contain contours of a single orientation show a diminished ability to resolve gratings of the orthogonal orientation in later life. It is argued that these perceptual deficits result from changes in the organization of the visual cortex induced by the selected early visual input.

Many of the properties of neurons in the visual cortex of cats and monkeys are influenced by the visual experience of the first 3 months of life (1-4). Dramatic demonstrations of this were provided by the studies of Hirsch and Spinelli (2) and Blakemore and Cooper (3), who restricted the visual input of each eye of young kittens to stripes of a single orientation (either vertical or horizontal). After several months of such rearing, all visual cortical neurons responded best to edges or bars having orientations similar to that of the contours to which each eye had been exposed. In the case of Blakemore and Cooper's kittens, which experienced contours of the same orientation in the two eyes during the first 5 months of life, no neurons at all could be found that had preferred orientations perpendicular to that of the contours in which they were reared. This distribution of preferred orientations is clearly very different from that found in normally reared cats, in which all orientations are equally represented (5).

It is possible that the properties of neurons in the human visual system are similarly susceptible to early visual experience. Humans with ocular astigmatism can be considered to have been "deprived" of sharp images of contours of certain orientations throughout the time that their refractive error was uncorrected. Even when the astigmatism is fully corrected with lenses, many adult astigmats show dramatically reduced acuity for gratings having the orientation that was habitually seen most blurred before correction (6). The argument that human visual resolution is influenced by early visual experience would be strengthened considerably if it could be shown that the physiological effects of selective visual deprivation in cats were accompanied by concordant deficits in visual acuity. In this report we provide evidence that cats selectively deprived of contours of certain orientations in early life do indeed show long-lasting and perhaps permanent deficits in their ability to perceive these contours as adults.

We reared three kittens using a procedure and environment virtually identical to that of Blakemore and Cooper (3); thereby we hoped to duplicate the physiological deficits they found. Each kitten was placed for 5 hours a day on a clear Plexiglas plate mounted in the middle of a cylinder 1.8 m high that had stripes of various widths but of a single orientation on the inside walls. The kittens wore ruffs around their necks to prevent them from seeing their own bodies, and whenever they were not in the cylinders they were kept in the dark. In this way their visual experience during the first few months of life was confined to edges of one orientation. Two of the kittens were reared from age 20 days until 5 months in cylinders with stripes that were vertical for one kitten (V_1) and horizontal for the other (H_1) . The third kitten (V_2) was reared in a cylinder with vertical stripes from age 3 weeks until 5 weeks. When the kittens were about 6 months old they were removed from the dark and placed in a normal lighted environment (7). After they had been in the light for from 3 to 6 months, their ability to resolve vertical and horizontal gratings was measured by the use of operant techniques developed by Berkley (8).

Each cat was initially induced to place its head into a cylinder of 12-cm diameter mounted at one end of an operant conditioning chamber, and to push with its nose one of two transparent Plexiglas keys mounted side by side above a food cup. They were then trained to discriminate between a square wave grating and a blank field of the same mean luminance (9) in a discretetrial simultaneous discrimination task. The discriminative stimuli, visible to the cat through the two transparent nose keys, were back-projected onto two circular screens 11 cm in diameter at a distance of 32 cm from the keys. Interposed between the keys and the screens were two cones that ensured that only one stimulus could be seen through each key. All gratings had a contrast close to 1.0 and a luminance of 75 cd/m². Whenever the cat pressed a key the stimuli were turned off; if it pressed the key behind which the grating was projected it received 0.4 ml of diluted beef baby food, and a new trial began 5 seconds later. If it pressed the other key it was not fed, and the intertrial interval was increased to 10 seconds; further consecutive errors resulted in 15-second intertrial intervals. Safeguards were included in the program to overcome position preference and to discourage the cat from pressing the keys during the intertrial intervals.

Daily sessions consisted of 80 trials with the gratings vertical and 80 trials with them horizontal. First the cats were trained on gratings with a spatial frequency of 0.22 cycle/deg, and were required to reach one of two criteria, either an average score of more

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than 90 percent correct on two consecutive days or an average score of more than 80 percent correct on four consecutive days. When the animal reached either of these criteria, the spatial frequency of the gratings was increased and the procedure repeated. Thereafter, the spatial frequency of the gratings was increased whenever either of these two criteria was reached or when performance was judged to be asymptotic for six consecutive days. We are certain that each cat made its discrimination using pattern rather than luminance cues, because their performances on the discrimination immediately



Fig. 1. The percentage of correct responses made by two normal and three visually deprived cats on a simultaneous discrimination between a grating and a blank field of the same mean luminance as a function of the grating spatial frequency; O, vertical gratings; •, horizontal gratings. When the performance was at a level of 80 percent or better, each point is based on either 160 or 320 trials. When the performance was below 80 percent, each point represents an average of 6 days (480 trials) of asymptotic performance. The spatial frequency of the grating was calculated by using the distance between the grating and the eye of the cat when its nose just touched the transparent response key. (A and B) Two normally reared adult cats exhibited negligible differences in their performance for vertical and horizontal gratings. (C and D) Cats reared in environments with vertical stripes throughout the first 5 months (V_1 , in C) or during the period between weeks 3 and 5 (V_2 , in D) showed near normal performance for vertical gratings but a clear deficit with horizontal gratings. (E) Cat H₁, reared in an environment with horizontal stripes throughout the first 5 months of life, showed a clear deficit in its performance when the gratings were vertical but normal performance when they were horizontal.

fell to chance when the pattern was removed by the insertion of pieces of diffusing material in the paths from the projectors to the screens. We also ascertained that the cats did not tilt their heads during either discrimination task.

Figure 1 shows the results for the three deprived cats together with similar data obtained from two normally reared control animals. In each graph, the mean percentage of correct responses over the days of asymptotic performance are plotted as a function of grating spatial frequency. The two normally reared cats (Fig. 1, A and B) exhibited no systematic differences in their performance for vertical and horizontal gratings. However, the performance of the deprived animals (Fig. 1, C to E) for test gratings exceeding 0.46 cycle/deg was clearly superior for the orientation that they experienced in early life (10). In fact, for spatial frequencies higher than 1.5 cycle/deg, there was virtually no overlap of the daily scores for the two grating orientations.

It is possible to obtain an estimate of the cutoff spatial frequency from these data on the assumption that this is the frequency at which the cat's performance is at chance (50 percent). The estimates for the two normal cats, 3.0 and 3.1 cycle/deg, are only slightly smaller than values obtained earlier (11)by behavioral means and estimates obtained from evoked cortical potentials (12), but fall well short of the cutoff spatial frequency for the optics of the cat eye (13). The values obtained from the deprived animals for gratings of the experienced orientation-3.4, 3.0, and 3.3 cycle/deg for V_1 , H_1 , and V_2 , respectively-are comparable to the estimates obtained from the normally reared cats. By contrast, the cutoff spatial frequencies for gratings of the corresponding orthogonal orientations were only 2.6, 2.45, and 2.0 cycle/deg, respectively. This suggests that the early selective visual experience of these cats resulted in consistent disparities of between 18 and 40 percent in the cutoff spatial frequencies for gratings of the experienced and its orthogonal orientation. The largest difference (40 percent) was observed in V2, which had been reared in the stripes for the shortest period. Interestingly, the physiological effects of deprivation also appear to be more pronounced with shorter exposures. Recent studies (4, 14) suggest that the distribution of preferred orientations of cortical neurons is more tightly clustered about the experienced orientation in animals whose exposure to stripes lasted only a few weeks rather than several months as in the original studies (3, 4).

The long-term behavioral deficits observed in our cats are considerably smaller than might have been expected from the dramatic temporary defects described by Blakemore and Cooper (3) when the cats are first exposed to a normal lighted environment. A similar conclusion was reached by Hirsch (15) from quite different behavioral tests. Our results show that the longstanding consequence of early selective visual deprivation is not a blindness for contours of the orientation orthogonal to those present in the early visual environment, but only a slight reduction in acuity, a result consistent with the deficits observed in many optically corrected human astigmats (6). There is good evidence that the acuity deficits we found are long-lasting. Although most of our cats have been in normal lighted environments for nearly a year, current repetitions of the curves of Fig. 1 have revealed no improvement in performance. This result is thus concordant with the recent finding (16) that, apart from changes in ocular dominance, the most dramatic physiological effects of deprivation remain largely unchanged even after nearly 2 years of normal visual exposure.

The results of our experiments indicate that the ability of the cat to resolve contours is influenced by its early visual experience. This finding provides strong support for the suggestion (6) that the meridional differences in acuity observed in optically corrected human astigmats as well as the lesser ones (for oblique orientations) observed in normal eyes result from certain asymmetries in the early visual input.

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 At first the kittens all showed the gross behavioral deficits described by Blakemore and Cooper (3) but most of these disappeared within between 12 and 16 hours of exposure to a lighted environment. However, the ability to strike or visually follow sticks held orthogonal to the experienced orientation remained poor in two cats for several weeks. While these cats learned within 16 hours to successfully strike at the stick when it was held at the rearing orientation, they either stopped responding to it or struck at it in a hesitant fashion when the stick was held orthogonal to this orientation.
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- 17. We wish to express our appreciation to M. Berkley for introducing us to his techniques for training cats and to F. Stefani for his excellent photographic services. Supported by National Research Council of Canada grant APA 7660 to D.E.M.
- 27 November 1972

Abstract. The rapid habituation of many neurons in the frog optic tectum to moving spots is presumed to underlie the behavioral habituation of the frog to repeated movement of prey objects. The "disinhibited" feeding of frogs after pretectal lesions is paralleled by the consistent failure of tectal neurons to ignore moving buglike stimuli.

Disinhibition of Tectal Neurons by Pretectal Lesions in the Frog

In the frog, the optic tectum provides a major interface between vision and action, receiving retinofugal fibers from the opposite eye (1) and discharging directly into brainstem and spinal motor centers (2). Furthermore, the tectum ap-